TABLE 5

	RTR tetramer	PBS	Statistics (Chi-square)
NUMBER OF EYES	16	16	
ULCER DEPTH			
No Ulcer	9	2	
Anterior	4	6	
Middle	0	3	
Posterior	2	4	
Descemetocele	1	1	
Perforation	0	0	
TOTAL ULCERS			
During expt	7 (43.8%)	14 (87.5%)	p=0.0046, very significant (RTR vs PBS)
End of expt (day 42)	6 (37.5%)	12 (75%)	p=0.0163, significant (RTR vs PBS)

Discussion

Alkali-injury to the eye degrades many proteins in all layers of the cornea by hydrolysis of peptide bonds and destruction of certain amino acids.[17] This degradation of cellular and extracellular corneal proteins directly releases two neutrophilic tripeptide chemoattractants.[5] Subsequent *in vitro* experiments identified these chemoattractants as N-acetyl-PGP and N-methyl-PGP and confirmed their chemotactic properties.[4] The acetylated tripeptide was the one more active. Intrastromal injection of synthetic N-acetyl-PGP or the ultrafiltered tripeptide chemoattractants into normal cornea demonstrated heavy neutrophil invasion to the injection site.[6] Taken together these findings substantiated the role of this tripeptide chemoattractant in triggering the early neutrophil response in the alkali-injured eye, confirming its importance as an inflammatory mediator.

Using the molecular recognition theory, RTR complementary peptides were designed and synthesized that were found to be inhibitors of N-acetyl-PGP. The capacity of these complementary peptides to inhibit polymorphonuclear leukocyte

polarization varied with the chemoattractant. The most potent complementary peptide, RTR tetramer, showed greater inhibitory potency for synthetic N-acetyl-PGP compared to the ultrafiltered tripeptide chemoattractants. This might be the result of non-specific interaction with the heterogeneous group of small peptides (100-1,000 MWt) known to be present in the latter sample. The additional fact that these complementary peptides did not inhibit LTB_4 activated polarization demonstrates that they are not directly acting on the neutrophil in a non-specific manner. The absence of LTB_4 inhibition and the scarcity of extracellular LDH release from all incubations confirms that RTR complementary peptides were not toxic to neutrophils. Finally, these results also indicate that N-acetyl-PGP binds to a different neutrophil receptor than LTB_4.

The molecular recognition theory (or complementary peptides) posits that the pattern of hydropathy of amino acids is a gross determinant of shape and rudimentary function of that peptide or protein.[7] Therefore, inverting this hydropathic pattern should result in a peptide with a complementary shape, since the same driving forces are involved, but in reverse orientation. Hence it is